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10/555,076	03/02/2006	Toshiyuki Takagi	SNKYO126512	3081

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CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC
1420 FIFTH AVENUE
SUITE 2800
SEATTLE, WA 98101-2347

EXAMINER

BETTON, TIMOTHY E

ART UNIT	PAPER NUMBER
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1617

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/555,076

Applicant(s)

TAKAGI ET AL.

Examiner

Timothy E. Betton

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-62 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed 20 November 2007 have been acknowledged and duly made of record.

In the previous Office Action filed 25 July 2007, applicants were required to amend instant claims 43-47 and 59-61 to read "A method" instead of "The method". The proper procedure for amending the claims is to insert "A" in the place of "The" for the instant claims *supra*. In accordance with the requirement, the term "A" which preambles "method" should be crossed-through and the term "The" should preamble "method" to adequately meet antecedent basis.

Thus, the 112, 2nd paragraph rejection is maintained over instant claims 43-47 and 59-61.

Additionally, applicants' amendments to instant claims 42 and 49-54 disclosing '*consisting essentially of*' is not defined, described and/or explained in the instant specification or the claims in such a way as to suggest possession of the invention. Based on the amendment, it is unclear as to what applicants' intend by the said amendment. The phrase '*consisting essentially of*' indicates an objective drawn to further narrowing the scope of the claim. However, this amendment is not substantially elucidated in the instant specification and support drawn to correlative data or comparative results in reference to "*consisting essentially of*" is absent in the instant specification.

The transitional phrases "comprising", "consisting essentially of" and "consisting of" define the scope of a claim with respect to what unrecited additional components or steps, if any, are excluded from the scope of the claim.

The transitional phrase “consisting essentially of” limits the scope of a claim to the specified materials or steps “and those that do not materially affect the basic and novel characteristic(s)” of the claimed invention. In *re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original) (Prior art hydraulic fluid required a dispersant which appellants argued was excluded from claims limited to a functional fluid “consisting essentially of” certain components. In finding the claims did not exclude the prior art dispersant, the court noted that appellants’ specification indicated the claimed composition can contain any well-known additive such as a dispersant, and there was no evidence that the presence of a dispersant would materially affect the basic and novel characteristic of the claimed invention. The prior art composition had the same basic and novel characteristic (increased oxidation resistance) as well as additional enhanced detergent and dispersant characteristics.). “A consisting essentially of” claim occupies a middle ground between closed claims that are written in a consisting of” format and fully open claims that are drafted in a comprising” format.”

PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also *Atlas Powder v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); *In re Janakirama-Rao*, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); *Water Technologies Corp. vs. Calco, Ltd.*, 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, “consisting essentially of” will be construed as equivalent to “comprising.” See, e.g., *PPG*, 156 F.3d at 1355, 48

USPQ2d at 1355 (“PPG could have defined the scope of the phrase consisting essentially of” for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention.”). See also *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1240-41, 68 USPQ2d 1280, 1283-84 (Fed. Cir. 2003) (Applicant’s statement in the specification that “silicon contents in the coating metal should not exceed about 0.5% by weight” along with a discussion of the deleterious effects of silicon provided basis to conclude that silicon in excess of 0.5% by weight would materially alter the basic and novel properties of the invention. Thus, “consisting essentially of” as recited in the preamble was interpreted to permit no more than 0.5% by weight of silicon in the aluminum coating.); In re *Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of “consisting essentially of,” applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant’s invention. In re *De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also *Ex parte Hoffman*, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) (“Although consisting essentially of” is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant’s burden to

establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of language.”).

Further, applicants’ attention is directed to the 103(a) rejection over instant claims 41-62. Applicants’ essentially argue that neither the Lohray nor Ikeda references describe, teach, or suggest in any way a method for either increasing adiponectin production or treating hypoadiponectinemia.

In response, applicants’ arguments are considered but are not found persuasive. The link between HMG-CoA reductase inhibitors and adiponectin is made obvious by the teaching of Lohray et al. and Ikeda et al. which when incorporated together along with the motivation of Schulze et al.

For evidentiary purposes, the state of the art is replete with embodiments and disclosures which primarily link adiponectin with metabolic syndrome which is thought to result from obesity and obesity-linked insulin resistance. Additionally, statin treatment improves insulin resistance in skeletal muscle. Studies have also been conducted to determine whether a statin may affect the myocardial expression levels of AdipoR1 and AdipoR2 (Kadowaki et al., Adiponectin and Adiponectin Receptors, Endocrine Reviews 26 (3): 439-451, especially, printed pages 1-41, especially page 1, see abstract; Saito et al., Statin reverses reduction of adiponectin receptor expression in infarcted heart and in TNF- α -treated cardiomyocytes in association with improved glucose uptake, Am J Physiol Heart Circ physiol 293: H3490-H3497, 2007, printed pages 1-13, see abstract). These current references further substantiate the teachings and methods of Schulze et al. (already made of record).

Applicants' claim of possessing the first demonstration that the administration of a HMG-CoA reductase inhibitors increase adiponectin production and is effective in treating hypoadiponectinemia is not substantiated in view of prior that clearly reads on claimed invention.

Applicants' summarily claim that the references fail to teach or suggest a method for increasing adiponectin production according to instant claim 41. However, the Examiner does not find this persuasive and is inclined to the contrary in that the references (already made of record) *do* adequately read on the claimed subject matter in addition to clearly pointing out the inventive objective of current invention.

The 112, 1st paragraph rejection is maintain with the exception of the portion drawn to prevention, which the applicant has adequately amended. Accordingly, the 103(a) rejection is maintained for reasons already made of record.

Claim Rejection –35 USC 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of the invention which are useful for inhibiting amyloidosis

in disorders in which such amyloid deposition occurs, does not reasonably provide enablement for compounds of the invention which are useful for inhibiting amyloidosis in disorders in which such amyloid deposition occurs such as diabetes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Exparte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988).

The factors to be considered in determining whether undue experimentation is required include: 1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The Board also stated that although the level of skill in the pertinent art is high, due to the multiplicity and variability of the diabetic disease state; whether type I or type II. While all these factors are considered, a sufficient amount for a *prima facie* case is discussed below:

The nature of the invention

The nature of the instant invention is highly complex.

The amount of direction or guidance provided

Applicants cite the limitation "consisting essentially of" in the instant claims.

However, there is nothing presented in the instant specification that lends guidance and/or direction as to how this amendment may be interpreted. The instant specification has not substantially explained reasoning as to what is the inventive objective sought via the disclosure "consisting essentially of". In the absence of any definition, description, or explanation drawn to the limitation "consisting essentially of" in view of claimed invention, a scope of enablement is lacking.

The quantity of experimentation necessary

As stated above, the nature of the instant invention is highly complex. Thus, amount of experimentation required in order to achieve the goals of the inventive objective of current invention is high. The invention is drawn to the administration to a certain target population which has not been adequately elucidated in any embodiments of the specification. In vitro testing and ex vivo testing in mice is routine experimentation, however the quantity and nature of experimentation, whether actual or representative (target population presenting with diabetic conditions) is deficient in order to determine a sufficient scope of enablement.

The predictability in the art

The unpredictability in the art is high due to the variable susceptibilities of the diseases states disclosed. There is no guidance in the specification as to how to determine and

select a population of individuals, which may or may not eventually have hypoadiponectinemia, metabolic syndrome, diabetes, and complications thereof. Preventing a disease is just as complex and unpredictable a process. It is not clear what parameters one skilled in the art would use in order to identify a population of subjects in which the disease could be prevented. It is also not clear what symptoms one of skill in the art would need to identify before possibly treating a patient. While it is art known that clinicians are capable of implementing both screening and surveillance and the type of screening test used and the intervals at which it is performed are based on risk stratification, which also serves as the basis for selecting potential candidates for possible prevention. However, like most screening procedures determining whether a population will eventually contract said disease is not foolproof. There is insufficient evidence provided enabling one of ordinary skill in the art to determine susceptible Syndrome X candidates within a population. The specification provides neither guidance on nor exemplification of identifying a population of people who may eventually have Syndrome X. Furthermore, if such a group was identified there is insufficient evidence provided that the metabolic syndrome/ diabetic event would be inhibited with the administration of one or more of a HMG-CoA reductase inhibitors.

Claim Rejection- 35 USC §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 41-62 are rejected under 35 U.S.C. 103(a) as being unpatentable Lohray et al. (USPN 6,130,214) in view of Ikeda et al. (USPN 6,384,062).

For exemplary purposes, the synthesis, properties and characteristics of adiponectin/adipocytes are well known in the pertinent art. Adiponectin, predominantly synthesized in the adipose tissue, seems to have substantial anti-inflammatory properties and to be a major modulator of insulin resistance and dyslipidemia, mechanisms that are associated with an increased atherosclerotic risk in diabetic patients (Schulze et al., Adiponectin and Future coronary Heart Disease Events Among Men with Type 2 Diabetes, Diabetes (2005), 54:534-539, printed pages 1-6).

Thus, instant referenced publication teaches adiponectin as a major modulator of dyslipidemia. The instant claims of alleged invention disclose HMG CoA reductase inhibitors, i.e., pravastatin and rosuvastatin in particular. These said agents are effective against dyslipidemia and conditions thereof. By virtue of the mechanism of action of agents such as pravastatin, adiponectin is likely to increase in instances as typical characteristic and property of HMG CoA- reductase inhibitors treatment.

Lohray et al. teach novel antiobesity and hypocholesterolemic compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and

pharmaceutically acceptable compositions containing them. More particularly, the present invention relates to novel .beta.-aryl-.alpha.-oxysubstituted alkylcarboxylic acids of the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them (Abstract).

Lohray et al. teach compounds useful in the reducing body weight and for the treatment and/or prophylaxis of diseases such as hypertension, coronary heart disease, atherosclerosis, stroke, peripheral vascular diseases and related disorders. These compounds are useful for the treatment of familial hypercholesterolemia, hypertriglyceridemia, lowering of atherogenic lipoproteins, very low-density lipoprotein (VLDL) and LDL. The compounds of the present invention can be used for the treatment of certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, and retinopathy nephropathy. The compounds of general formula (I) are also useful for the treatment/prophylaxis of insulin resistance (type II diabetes), leptin resistance, impaired glucose tolerance, dyslipidemia, disorders related to syndrome X such as hypertension, obesity, insulin resistance coronary heart disease, and other cardiovascular disorders. These compounds may also be useful as aldose reductase inhibitors, for improving cognitive functions in dementia, treating diabetic complications, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), inflammatory bowel diseases, osteoporosis, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma and for the treatment of cancer. The compounds of the present invention are useful in the treatment

and/or prophylaxis of the above said diseases in combination/concomittant with one or more HMG CoA reductase inhibitors or hypolipidemic/hypolipoproteinemic agents such as fibric acid derivatives, nicotinic acid, cholestyramine, colestipol, probucol (column 1, lines 43-67; column 2, lines 1-6).

Ikeda et al. teach a pharmaceutical composition which comprises an insulin sensitivity enhancer in combination with other antidiabetics differing from the enhancer in the mechanism of action, which shows a potent depressive effect on diabetic hyperglycemia and is useful for prophylaxis and treatment of diabetes (Abstract).

Ikeda et al teach the administration of pravastatin and its sodium salt, which is interchangeable with the 'water soluble' limitation in instant claims of subject invention.

Ikeda et al. teach the administration of pravastatin for the disease states and conditions, which make the embodiments in instant specification and instant claims obvious (column 18, lines 21- 22; lines 35- 36).

Thus, it would be prima facie obvious to one of ordinary skill in the pertinent art to at once recognize at the time of invention the reasonable expectation of success via the combining of the compositions and methods of Lohray et al. with the compositions and methods of Ikeda et al. Ikeda et al. teaches the motivation to incorporate together, thereby making the claim of instant invention obvious.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access

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SHENGJUN WANG
PRIMARY EXAMINER

TEB